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Indomethacin for prevention of ectopic ossification after hip arthroplasty

Twelve patients at risk of developing postoperative para-articular ossifications were treated with indomethacin. Ossification after previous total hip arthroplasty was excised in eight patients. Four patients had ossification in the opposite hip after previous arthroplasty. Five patients in whom ectopic ossification was excised developed recurrences of lesser degree than the primary ossifications. One patient with the condition in the opposite hip developed ossification. No patients complained of stiffness in the hip and all had markedly increased hip motion. Indomethacin seems to be valuable as prophylaxis in patients at risk of developing ectopic ossification and as a supplement to secondary excision.

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Para-articular ectopic ossification is a well-known complication of hip arthroplasty (Nollen & Slooff 1973). Reports on the incidence vary from 15 to 90 per cent (Delee et al. 1976, Rosendahl et al. 1977), depending in part on classification of the condition.

There is no documented, satisfactory treatment for the condition, but several methods have been tried as prophylaxis. Bijvoet et al. (1974) found that disodium ethane-1-hydroxy-1, 1-diphosphonate did not prevent the development of ossifications, but it delayed mineralization of the ectopic bone matrix. Coventry & Scanlon (1981) used irradiation of the hip postoperatively; after excision, 67 per cent had a moderate recurrence and 33 per cent remained free of ossification. Riska & Michelsson (1979) and Abrahamsson et al. (1984) showed in six and four patients that insertion of free fat transplants after secondary excision prevented recurrence in 50 and 25 per cent of cases, respectively.

Our study was based on the observations of Dahl (1975), who drew attention to the possible prophylactic effect of indomethacin on ossification following THA, and Lidgren & Nordström (1979) and Ritter & Gioe (1982), who used the drug after excising ossifications in one and six hips, respectively; the condition did not recur in any of these hips.

Patients and methods

Eight patients, who had undergone hip arthroplasty a.m. Lubinus 5–54 months previously and had developed symptomatic ossifications, had these ossifications excised. Seven patients were men and all had primary arthrosis; the eighth patient was a female with failed Monk arthroplasty after femoral neck fracture (Table 1). Prior to the excision all patients claimed stiffness in the hip, and all but two had pain at rest and/or on walking. They were treated with peroral indomethacin (Confortid®) 25 mg three times daily postoperatively for 6 weeks. The drug had to be withdrawn in two patients after 6 and 7 days due to dyspepsia and postoperative hepatic insufficiency, respectively.

Four patients had previously developed ectopic ossifications after hip arthroplasty and were now being operated a.m. Lubinus in the opposite hip because of primary arthrosis in three patients and failed Ring arthroplasty in the fourth (Table 2). All were treated with indomethacin, as above.

All hips were operated by a posterolateral approach. The follow-up time was 6–18 months.

The degree of ossification was assessed radiographically according to DeLee et al. (1976): Grade 1: Para-articular ossifications occupying less than 50 per cent of the distance between femur and pelvis; Grade 2: Para-articular ossifications occupying more than 50 per cent of, but not bridging the distance between femur and pelvis; Grade 3: Bridging ossifications.

Table 1. Patients treated with excision of para-articular ossifications (PO) and indomethacin after previous total hip arthroplasty (THA). Range of motion is a sum of extension-flexion, abduction-adduction and rotation in the hip. PO was graded from 0–3 according to DeLee et al. (1976)

Case	Sex	Age at THA (yr)	Interval THA-excision (mo)	Degree of PO			Range of motion		Latest follow-up (mo)
				Before excision	At 3-month follow-up	At latest follow-up	Before excision	At latest follow-up	
1	M	71	33	3	1	1	110	210	18
2	M	61	30	3	0	1	50	210	18
3	M	59	6	3	0	1	45	230	16
4	M	64	21	2	0	0	120	200	12
5	F	88	5	3	0	0	0	175	11
6	M	68	35	3	2	2	10	95	6
7	M	60	54	3	2	2	15	135	16
8	M	78	8	3	0	0	90	175	7

Results

In eight patients with excision, five developed new Grade 1 or 2 ossifications. In three patients ossifications were visible within 3 months but did not progress. In two patients recurrences occurred after 3 months (Table 1). Two patients who developed new ossifications had the drug withdrawn prematurely. All patients had improved hip motion. None of the patients complained of stiffness in the hip, but one patient had pain in the hip when sitting

One of four patients with ossifications after contralateral THA developed a Grade 2 condition in the other hip, observed at the 1-year follow-up (Table 2). No patients complained of stiffness or pain in the hip.

Discussion

Symptomatic para-articular ossification, i.e. pain in the hip on moving and/or resting and severe stiffness, has been reported in 2–5 per cent of total hip arthroplasties (DeLee et al. 1976, Ritter & Vaughan 1977, Kromann-Andersen et al. 1980, Kjærsgaard-Andersen & Schmidt 1984). High frequencies of recurrence have been observed after secondary excision (Ritter & Vaughan 1977, Fahmy & Wroblewski 1982). A 90 per cent recurrence rate was found in cases with contralateral ossifications (DeLee et al. 1976).

In three of eight patients with excision followed by indomethacin treatment for 6 weeks, we found minor non-progressive recurrences at the 3-month follow-up. In two patients we found mild ossifications developed after the third month. Of four patients with a high risk of developing ossifications after THA in the second hip, only one developed a Grade condition, disclosed at the 13-month follow-up. The number of patients in our study was small, but all were at risk of developing ectopic ossifications.

Rø et al. (1976) and Sudmann & Bang (1979)

Table 2. Four patients with para-articular ossifications (PO) in the opposite hip after total hip arthroplasty (THA) and with postoperative indomethacin prophylaxis after THA in the second hip

Case	Sex	Age at second THA (yr)	Interval THA-THA (mo)	Degree of PO in opposite hip	Degree of PO in second hip		Latest follow-up (mo)
					At 3 month follow-up	At latest follow-up	
1	M	64	12	3	0	0	18
2	M	77	16	2	0	0	16
3	M	73	4	3	0	2	13
4	M	71	6	3	0	0	12

demonstrated the inhibitory effect of indomethacin on periosteal fracture healing in rats and on the remodelling of Haversian canals. Almåsbakk & Røysland (1977) published a study of 81 hip operations in which indomethacin had been given postoperatively in one third. They found no difference between the two groups with regard to the frequency of milder degrees of ossifications, whereas there were fewer cases of the severest degrees in the indomethacin group. This is in accordance with our results.

The fact that ossifications developed after the third month could indicate that indomethacin treatment has only a delaying effect. However, since no severe ossifications developed during the follow-up as expected (DeLee et al. 1976), a true inhibitive effect of the drug may be postulated. It has been proposed that the effect of indomethacin is attributable to the inhibition of prostaglandin synthetase activity (Vane 1971), which also affects bone metabolism (Dietrich & Raisz 1975, Schelling et al. 1980, Farr et al. 1984). Rane et al. (1978) found a considerable inter-subject variability in the blocking effect of indomethacin on prostaglandin synthesis with maximal inhibition after a daily dose of 75–150 mg. These observations suggest that our dosage was too low to prevent new ossifications in all patients.

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